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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/774,178	02/01/2001	Tetsuya Ishizuka	P66351US0	7485

136 7590 07/20/2006

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EXAMINER

WILDER, CYNTHIA B

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 07/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/774,178

Applicant(s)

ISHIZUKA ET AL.

Examiner

Cynthia B. Wilder, Ph.D.

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 May 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11 and 19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendment filed May 8, 2006 is acknowledged and has been entered. Claims 11 and 19 have been amended. Claims 11 and 19 are pending. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejection

3. The prior art rejection under 35 USC 103(a) is maintained and discussed below.

Claim Rejections - 35 USC § 103

Issue: The claims 11 and 19 are rejected under 35 USC 103(A) as being unpatentable over Nakahara et al in view of Kievits et al and further in view of Leone et al and Malek et al.

Applicant's traversal

4. Applicant traverses the rejection on the following ground: The rejection relies on four, separate prior art references. Applicant states that each of the cited references separately discloses limitations found combined in the present rejected claims. Applicant summarizes the examiner's rejections and states the rejection is incorrect. Applicant further cites case law on the requirements for obviousness and asserts that the alleged motivation for combining the cited references fail to satisfy the standards for showing the requisite prior art motivation needed to sustain a rejection under 35 103(a). Applicant states that with respect to the alleged motivation

Art Unit: 1637

for combining the separate prior art teaching, the rejection merely relies on the fact that methods disclosed in the cited references are similar to one another. Applicant states that it establishes not more than the fact that the limitations found in the references were known, separately, in the prior art; which, at best, supports a finding that it would have been obvious to try various combinations. Applicant states that the fact that all elements of the claimed invention are known does not, by itself, make the combination obvious. Applicant states that the requisite "desirability" and thus the obviousness, of making the combination being absent from the cited references, lack of patentability based on the cited references has not been demonstrated. Applicant states that the PTO tries to use the claims as a frame and the prior art references as a mosaic to piece together a facsimile of the claimed invention which is impermissible in an obviousness analysis under 103(a). Applicant further states that with respect to reliance on the claim limitations being "highly desirable" optimization of features disclosed in the cited references, this renders the rejection "inadequate on its face." Applicant states that the optimization of a claim variable was not recognized in the art as effecting the claimed result, the result is unobvious. Applicant states that a difference with the prior art amounts to an alleged "optimal condition...is not a substitute for some teaching or suggesting supporting an obviousness rejection.

Applicant states that furthermore, the rejection fails to take account disclosure in the cited reference that appear to teach away from the present claims. Applicant states that in the accordance with the presence rejected method claims, target RNA is efficiently amplified (using a T7 promoter in tris-HCL buffer) in the presence of, i.e., "3.2 to 4.4 mM" inosine triphosphate in terms of the final concentration. The rejection relies on modifying Nakahara in view of Kievits, but the fact remains that Nakahara and Kievits disclose optimal ITP concentrations for

Art Unit: 1637

RNA amplification at 2.0 mM and 2.5mM respectively. As such, since "a person of ordinary skill upon reading the reference would be led to use an optimal maximum ITP concentration of 2.5, which in a direction divergent from the path that was taken by the Applicant, i.e., using a minimum ITP concentration of 3.2 mM, the reference teaches away from the presently claimed invention. Applicant states that furthermore, these teaching of the optimal ITP concentration by Nakahara and Kievits means that RNA amplification is inhibited at final ITP concentrations higher than the optimal ITP concentrations taught by the cited references as set forth in the previously filed amendment. Applicant states that thus from the teachings by Nakahara and Kievits, one of ordinary skill in the art would never expected that RNA would be amplified more efficiently at ITP concentrations higher than the optimal ITP concentrations taught by Nakahara and Kievits. Applicant states that the properties exhibited by a claimed invention must be taken into consideration. Applicant states that moreover from the data show in the present application Figs. 7 and 8, it appears that improvement in amplification efficiency, in the presence of from 3.2 to 4.4 mM ITP, results in a trivial shortening of the rising time only by a couple of minutes. Applicant request the rejection be withdrawn.

Examiner's Response

5. All of the arguments have been thoroughly reviewed and considered: In response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In this case, the primary reference of Nakahara et al provides all of the limitations of the claims except for the teaching of the repeating steps using transcribed RNA in the presence of a fluorescently labeled probe and wherein the buffer Tris-HCl is present at final concentration of 50 mM to 80mM. The secondary reference of Kievits et al provides a similar teaching to that of Nakahara and further teaches the repeating steps using transcribed RNA. Kievits et al do not teach Tris-HCl buffer in a final concentration of 50 mM to 80 mM or the presence of a fluorescently labeled probe. The tertiary references of Leone et al and Malek et al provides a similar teaching to that of Nakahara further teach the used of a fluorescently labeled probe that hybridizes with the transcribed RNA. The references do not teach Tris-HCl in a final concentration of 50 mM to 80 mM, but rather teach obtaining a stock solution of Tris-HCl at a concentration of 200mM having a pH 8.5 and varying the buffer concentration to optimize RNA detection conditions. The tertiary reference of Malek et al further supports the teaching of Leone by teaching the preparation of a 1M stock solution of tris-HCL having a pH of 8.5 and 1 M stock of Magnesium chloride. Malek teach that these stocks can be diluted to obtain varying concentration to optimize the conditions of the RNA detection and amplification and thus

Art Unit: 1637

provides motivation for using concentrations of a buffer, tris-HCL at concentrations of 50mM to 80mM.

In response to applicant's arguments that the rejections which relies on modifying Nakahara in vie of Kievits teaches away from the instant invention because they disclose optimal ITP concentrations for RNA amplification at 2.0 mM and 2.5mM respectively, the examiner respectfully disagree. Specifically, the primary reference of Nakahara does not teach an optimal concentration of ITP at 2.0 mM and 2.5 mM as argued by Applicant, but rather teach the use of ITP at a concentration of 0-4mM (see page 1855, legend to Figure 1) which falls within the range claimed by Applicant. MPEP states that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235(CCPA 1955) (MPEP 2144.05). Thus, Applicant's arguments concerning the cited prior art teachings of the use of ITP at a concentration of 2.0 mM to 2.5 mM in the RNA amplification reaction is deemed moot in view of the teachings of Nakahara et al. Applicant's arguments are not sufficient to overcome the prior art rejections under 35 USC 103(a). Accordingly, the prior art rejection is maintained.

Conclusion

6. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

Art Unit: 1637

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit 1637



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